

ABSTRACTS

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SYPHILIS (General)

A Study of Syphilis and Sexual Habits in Greenland.

MARCUSSEN, P. V., and RENDAL, J. (1950). *Amer. J. Syph.*, **34**, 144.

The rarity of syphilis among the inhabitants of Greenland renders an epidemiological study of a recent outbreak of great interest.

In 1947 syphilis was introduced, by a man with early infectious syphilis, into an isolated community of 103 adults (60 women, 43 men) which had been free from syphilis for many years. On recognition of the spread of infection the settlement was completely isolated by the prohibition of all external traffic. All persons over 12 years of age were clinically and serologically examined each week until 9 weeks after the last infected person had been segregated.

The originator of the epidemic had had intercourse, over a period of 5 months, with seven women of whom four became infected. These four women had intercourse with fourteen other men of whom only one became infected; he in turn had intercourse with three women, none of whom developed syphilis.

After rigid quarantine of the settlement two methods of case finding were used: mass blood-testing and contact tracing. The mass blood-testing gave no result that had not already been achieved by contact tracing. In contrast to earlier reports, no particular immunity among Greenland people was found. *V. E. Lloyd*

Delayed Withdrawal Reflex and Perception of Pain: Studies in a Case of Syphilitic Meningomyelitis and Tabes with Extensor Plantar Responses of a Type not previously described. ASHBY, M. (1949). *Brain*, **72**, 499.

A detailed study is presented of the plantar responses in a case of paraparesis due to syphilis. Measurements were made of delayed pain perception, and the components of the plantar response were recorded. The findings are discussed at length. *P. W. Nathan*

A Case of Gumma of the Lung. (Un caso de sífilis gomosa pulmonar.) SANCHEZ-BARRIGA CARAPETO, M. (1949). *Actas. dermosif.*, **41**, 147.

Another Case of Tertiary Syphilide Following Trauma. (Un caso mas de sífilide terciaria traumática.) TOME BONA, J. M. (1949). *Actas. dermo-sif.*, **41**, 219.

SYPHILIS (Therapy)

Penicillin in the Treatment of Experimental Syphilis of Rabbits. V. The Synergistic or Additive Activity of Penicillin Injected Intramuscularly with Sodium Iodide Administered Orally and Intravenously. KOLMER, J. A. (1950). *Arch. Derm. Syph., Chicago*, **61**, 49.

As penicillin has pronounced synergistic activity when given conjointly with oxphenarsine and with bismuth in the treatment of experimental syphilis of rabbits, the author re-studied the spirochaeticidal activity of iodides alone, and the question of their synergistic action with penicillin.

He found that the minimal curative dose of penicillin, intramuscularly twice daily for 8 successive days, in the treatment of acute syphilitic orchitis of rabbits, was 500 units per kg. per dose, to a total of 8,000 units. Sodium iodide 0.025 to 0.1 g. per kg., given intravenously twice daily for 8 successive days to a total of 0.4 to 1.6 g. per kg., was slightly spirochaeticidal but not curative, and the same was true of 0.05 g. to 0.15 g., taken orally twice daily for 8 successive days to a total of 0.8 to 2.4 g. per kg.

However, administration of 250 units of penicillin per kg. intramuscularly twice daily for 8 successive days to a total of 4,000 units per kg., together with sodium iodide orally or intravenously twice daily for 8 successive days in doses of 0.1 g. per kg. to a total of 1.6 g. per kg., was completely curative.

Therefore, it appears that penicillin and iodides act synergistically or additively in the treatment of experimental syphilis. The author advocates the administration of potassium iodide orally three times a day, together with penicillin, in both acquired and congenital chronic or late cases of syphilis. *T. Anwyl-Davies*

The Treatment of Acute Syphilitic Orchitis and Generalized Syphilis of Rabbits with Repository Penicillin Products Alone and in Combination with Mapharsen and Bismuth Salicylate. KOLMER, J. A. (1950). *Amer. J. Syph.*, 34, 45.

Experimental syphilis in rabbits is much easier to cure than syphilis in human beings and less penicillin per kg. bodyweight is required, but data from experimental syphilis may nevertheless have some practical application in treatment of human syphilis. The author reports the results obtained with four repository penicillin compounds in 8-day and 15-day courses of treatment of acute syphilitic orchitis and generalized syphilis of rabbits inoculated with the Nichols-Hough strain of *Treponema pallidum*. The four compounds used were penicillin G sodium in refined peanut oil and bleached beeswax, procaine penicillin G in aqueous suspension, procaine penicillin G in sesame oil, and procaine penicillin G in refined peanut oil with 2 per cent. aluminium mono-stearate. Variations in curative activity were noted, probably due to the fact that the delaying action of the vehicle resulted in different levels of penicillin in the blood; procaine penicillin G was found to be as effective therapeutically as penicillin G sodium suspended in peanut oil and beeswax.

"Mapharsen" (oxophenarsine hydrochloride) by intravenous injection and bismuth salicylate intramuscularly were shown to have a synergistic action when combined with the penicillin compounds, this effect being greater with the arsenical. The author also states that iodides likewise show a synergistic action with penicillin compounds in rabbit syphilis, and believes that iodides by mouth should still be given in the latent and late stages of human syphilis. The full details and results of these interesting experiments do not lend themselves to summarization. S. M. Laird

Fatal Reactions to Arsenicals. [In English.] PIRILÄ, V. (1949). *Ann. Med. intern. fenn.*, 38, 177.

In a series of 385 cases treated over a period of 25 years at the Dermato-Venereological Clinic of Helsinki University, one or more complications followed arsenical therapy. The complications are probably representative of the severe reactions seen during these years in Finland. There were eleven deaths, eight occurring in females and three in males. Ten of these eleven had never received more than ten injections—usually of neoarsphenamine—each; one had received "solusalvarsan". All those who died had had dermatitis; four also had liver damage; one had had an encephalopathy in addition to the other two features mentioned. Some of the patients examined had had a temporary eosinophilia.

The author describes the case of a woman who died in 1926 after neoarsphenamine injections. The patient had had what appears to have been a "low colour-index anaemia" and icterus. At necropsy a severe toxic hepatitis, fatty degeneration of the heart, a toxic nephrosis, hyperplasia of the spleen, and a haematoma of the renal pelvis were found. The author points out the changes which have taken place in the views on aetiology and pathology during the 25-year period under

review, especially insofar as the liver is concerned. [Hence the difficulty of assessing the value of some of the opinions given, of the state of that organ in the cases analysed.] I. H. Milner

The Effects of Crystalline Penicillin G and of Impure Penicillin on Experimental Syphilis. (Effets de la pénicilline G cristallisée et des pénicillines impures dans le traitement de la syphilis expérimentale.) LEVADITI, C., VAISMAN, A., and HAGEMANN, G. (1949). *Pr. méd.*, 57, 1249.

The antisymphilitic efficacy of crystalline penicillin G and of two impure penicillin preparations was compared in rabbits with scrotal syphilomata, and infected mice. Adequate doses of penicillin were given by subcutaneous injection and the effect on the rabbits assessed in respect of time of disappearance of treponemes from scrotal lesions, speed of healing, and sterilization of the lymphatic system as demonstrated by lymph-node transfer to other rabbits. The mice, infected for 305 days, were killed after 22 to 25 days' treatment and the presence or absence of treponemes in the zones of election compared with the findings in controls. Contrary to previous reports the antisymphilitic activity of the impure penicillins was not shown to be superior to that of pure crystalline penicillin G in these animals. James Marshall

Chloramphenicol and the Venereal Diseases. WILLCOX, R. R. (1950). *Brit. med. J.*, 1, 467.

The author, working in Southern Rhodesia with very limited supplies of chloramphenicol, treated four patients with early syphilis, two of whom were in the primary and two in the secondary stage. The total dosage given ranged from 1.75 g. to 3 g., and the period of administration from 3 to 5 days. In three patients dark-field examination became negative within 24 hours and in the fourth at 72 hours. All reached the stage of apparent clinical cure, which was achieved in an average time of just under 7 days. Two patients with gonorrhoea were also apparently cured, one of whom had prostatitis and an abscess of Cowper's gland. The total dose in the uncomplicated case consisted of one capsule of 0.25 g., while the other patient received one capsule twice daily for 3½ days.

It is of interest that three of the syphilitic patients were inoculated with bubo fluid from a known case of chancre immediately before treatment with chloramphenicol and that they failed to develop any lesion at the site of inoculation. G. L. M. McElligott

The Treatment of Neurosyphilis by the Intradermal Injection of Penicillin. (Sul trattamento intradermico della penicillina nella neurologia.) PINTUS, G. (1949). *Sistema nerv.*, 1, 16.

Nine cases of neurosyphilis were treated by intradermal injections of penicillin in small doses. The patients received daily injections of 40,000 units of penicillin in beeswax and arachis oil for a period of 25 to 30 days. A favourable change in the serological reactions in blood and spinal fluid is reported. The clinical results are regarded as excellent and the author states

that they compare well with those obtained with massive doses of penicillin by the intramuscular route.

Kate Maunsell

Penicillin and Fever Therapy in Early Syphilis. A Report of 161 Patients Treated with 2.4 Million Units of Penicillin and Physically Induced Fever. PLOTKE, F., SCHWEMLEIN, G. X., CRAIG, R. M., and RODRIQUEZ, J. (1950). *Amer. J. Syph.*, **34**, 161.

A group of 148 cases of early syphilis was treated with 2,400,000 units of penicillin in $7\frac{1}{2}$ days and three 3-hour sessions of artificial fever at 106°F . (41.1°C .) on alternate days during that period. The cumulative failure rate at 12 to 15 and at 24 to 27 months is reported. The results in the group of 95 cases of secondary syphilis thus treated are compared with those in 266 cases treated with a similar course of penicillin alone. The difference in the results of the two schedules suggests that the addition of fever therapy increases the effectiveness of penicillin.

V. E. Lloyd

Treatment of Early Syphilis with Penicillin and Bismuth Subsalicylate. Daily Injection of 500,000 Units of Penicillin G in Sodium Chloride Solution for Twenty Consecutive Days and Ten to Twenty Doses of Bismuth Subsalicylate at the Rate of Two a Week. PARDO-CASTELLO, V., and PARDO, O. A. (1950). *Arch. Derm. Syph.*, Chicago, **61**, 196.

A series of 47 patients with early syphilis, of whom 34 per cent. were male Negroes, 20 per cent. Negresses, and 40 per cent. male white persons, and of whom 17 per cent. had serum-negative primary syphilis, 42.5 per cent. serum-positive primary syphilis, and 40.5 per cent. secondary syphilis, were treated by daily injections of penicillin in aqueous solution together with bismuth given over a longer period. The dose of penicillin was ten million units administered in daily injections of 500,000 units over 20 days, and bismuth salicylate was given twice weekly for 10 to 20 weeks to a total of 1.3 to 2.6 g. The patients actually received penicillin daily for 20 days and bismuth treatment for from 15 to 50 days longer.

Six patients defaulted and the remaining 41 were followed up for from 3 to 15 (average 6) months. At the time of the report 26 (63.4 per cent.) had maintained or attained serum-negativity, the serum positive-cases taking an average of 74 days to become serum-negative. The remaining fifteen patients were progressing satisfactorily with a declining serological titre. There were no relapses.

R. R. Willcox

Comparison of Oral Penicillins. BOGER, W. P., BEATTY, J. O., and FLIPPIN, H. F. (1949). *Trans. Stud. Coll. Phys. Phila.*, **17**, 105.

To each of six subjects five different preparations of penicillin were given orally, and sodium penicillin intramuscularly in single doses of 200,000 units and the plasma penicillin concentration over the next $3\frac{1}{2}$ hours estimated and compared. The preparations given by mouth consisted of sodium, potassium, and aluminium salts of penicillin, and procaine penicillin (two differently

buffered potassium penicillin preparations being included). Widely differing results were obtained. The aluminium penicillin preparation with a sodium benzoate buffer gave significantly higher plasma concentrations than any of the other oral preparations. With this preparation the ratio of the plasma penicillin concentration after intramuscular to that after oral administration was 14 : 1 half an hour after administration, 3 : 1 at $1\frac{1}{2}$ hours, and 1 : 1 at $2\frac{1}{2}$ and $3\frac{1}{2}$ hours. With the other preparations the half-hour figures were as high as 35 : 1, and did not fall below 3 : 1 at $3\frac{1}{2}$ hours. Over a $3\frac{1}{2}$ -hour period, one-sixth as much penicillin was recovered in the urine after oral as after intramuscular administration. The authors point out that although this series is a small one, the conditions were rigidly controlled, and their figures have been subjected to statistical analysis and found to be highly significant.

A. W. H. Foxell

The Use of Procaine Penicillin with Aluminium Monostearate in Adults. WAYNE, E. J., COLQUHOUN, J., and BURKE, J. (1949). *Brit. med. J.*, **2**, 1319.

The concentration of penicillin in the serum of adult patients and volunteers after the injection of procaine penicillin in arachis oil with 2 per cent. aluminium stearate has been studied by the authors at the Sheffield Royal Infirmary. The serum penicillin level was estimated by comparing the effect of serial dilutions in phenol-red-glucose-serum medium upon *Streptococcus pyogenes* with that of similar dilutions of standard penicillin.

After a single injection of 300,000 units, the maximum concentration of penicillin in the serum was reached in about 3 hours, and a bacteriostatic level of more than 0.06 unit per ml. was maintained for 24 hours in nine out of ten cases. In two patients with impaired renal excretion a level of 2 to 4 units per ml. was found at the third hour. A further 33 patients received a single dose of 600,000 units and in all cases the serum penicillin level was maintained above 0.06 unit per ml. for 24 hours and above 0.03 for 48 hours. Even after 72 hours the level in 24 out of 29 patients remained above 0.03 unit per ml., and the average for the whole group was above 0.06. Three patients were given 600,000 units crystalline penicillin G in aqueous solution for comparison; the serum level fell below 0.03 unit per ml. in 10 hours. Daily doses of 600,000 units procaine penicillin with 2 per cent. aluminium stearate were then given for 4 days to fifteen patients: an almost constant serum penicillin level of 0.125 to 0.5 unit per ml. was maintained during treatment. The most constant levels were found when preparations containing the penicillin in particles less than 5μ in diameter were used. When caronamide (4 g. every 4 hours) was also given (in one case), the blood concentration of penicillin attained was higher than with the penicillin preparation alone.

The authors review the arguments for and against the discontinuous administration of large doses of penicillin and conclude that the balance of evidence is in favour of maintaining a steady blood level, such as that given by daily doses of 600,000 units procaine penicillin with

2 per cent. aluminium stearate. Single daily doses also save time in nursing and cause less discomfort to the patient. A daily "peak" concentration may be superimposed upon the steady blood level by adding soluble penicillin to the injection if desired. *L. G. Goodwin*

Aureomycin in the Treatment of Syphilis. (L'auroéomycine, nouvelle médication anti-syphilitique.) LEVADITI, C., and VAISMAN, A. (1950). *Pr. méd.*, **58**, 333.

In this paper an attempt is made to assess the value of aureomycin as an antisyphilitic drug. Previous work with clinical cases and in experimentally infected rabbits is discussed in some detail. If the disappearance of spirochaetes from films and the healing of chancres are taken as criteria, aureomycin, given orally or by intramuscular injection, has definite therapeutic properties but is slow in action compared with bismuth, arsenic, or penicillin. The authors point out that the paucity of accurate serological data makes an estimate of absolute cure after aureomycin therapy impossible. Anorexia, nausea, and vomiting, between the 2nd and 5th days of treatment appear to be frequent side-effects.

Personal experiments with aureomycin in experimentally infected animals are described. They have worked with rabbits and mice [the number of animals is unspecified]; results are given in the case of five rabbits with scrotal chancres and "a series" of mice. Two rabbits were given a total of 640 mg. per kg. by mouth in 5 days; spirochaetes disappeared [presumably from the chancre—no description of the test is given] in 10 and 13 days respectively, and the chancre healed in 15 days in both. The 3rd and 4th rabbits were given 200 mg. per kg. on two successive days by intramuscular injection, an aqueous suspension being used in one case and a suspension in arachis oil in the other. In the former animal spirochaetes disappeared in 5 days, in the latter in 24 hours, and healing of the chancre was complete by the 7th day in both. No relapses were observed in any of the animals during the time they survived. Similar results were obtained when a 5th rabbit was given 500 mg. per kg. in arachis oil by intramuscular injection on 3 successive days. A further test of cure was made by inoculating two groups of three healthy rabbits subscrotally with material from the popliteal glands of two of the infected animals. None of the test animals showed any sign of infection up to 35 days. It is noted that the use of the oily suspension caused the death of some animals a few weeks after treatment and in others gave rise to necrosis at the site of injection. To test the effect of aureomycin in clinically latent infection, mice were inoculated subcutaneously with fragments of syphiloma from infected rabbits, and 7 months later given either 20 mg. daily for 5 successive days by mouth or 40 mg. on two successive days by intramuscular injection. Seven days later the "elective sites" of nose and rectum were examined. No spirochaetes were found in the treated series and numerous spirochaetes in untreated series [no figures are given].

The authors conclude that aureomycin, though having definite antisyphilitic properties as judged by the criteria mentioned, is not likely to be of great value in the

treatment of syphilis, except possibly in cases of resistance to the usual agents. In this they confirm the opinion of previous workers. *E. A. Brown*

Treatment of Syphilis with Aureomycin Administered by Mouth. KIERLAND, R. R., HERRELL, W. E., and O'LEARY, P. A. (1950). *Arch. Derm. Syph., Chicago*, **61**, 185.

Two patients with dark-field-positive early syphilis were given orally 44.2 and 67.5 g. aureomycin respectively over 15 days. The results of dark-field examination became negative 16 and 60 hours after the onset of treatment and the sores healed within 2 weeks. The serum Wassermann reactions, which were negative at 38 to 40 days, remained so for the 172 and 296 days of observation.

A third patient, with a nodulo-ulcerative gumma of the right leg and with aortic regurgitation, received 56.5 g. over 18 days. The skin lesions began to heal on the fifth day. After 69 days the skin lesions had completely healed; there was no change in the aortic regurgitation, but the titre of the quantitative Kahn reaction of the serum had declined from 128 to 64 units. A fourth patient, a man with a nodulo-ulcerative gumma of the right forearm, received 60 g., the daily dose being somewhat limited by nausea and vomiting. The lesions had significantly improved by the end of 2 days and subsequently completely healed.

Three cases of neurosyphilis were also treated with aureomycin orally. In one, after malaria and bismuth administration and fever cabinet therapy, there were signs of relapse in the cerebrospinal fluid. Two patients were given 90.5 and 63.5 g. respectively over 28 and 31 days but the particulars in the third case are not recorded. The cerebrospinal fluid was studied for 198, 42, and 117 days respectively. During this time the lymphocyte count decreased from 18 to 3 cells per c.mm. in the first, 97 to 7 in the second, and 110 to 8 in the third. The total protein content likewise decreased from 60 to 25 mg. per 100 ml. in the first, from 100 to 60 in the second, and from 100 to 55 in the third. In one case the Kolmer and colloidal gold reactions changed from strongly positive to doubtful, but there were only slight changes in the others.

When 250 mg. aureomycin was given every 4 hours, or 500 mg. every 6 hours, levels in serum varied between 2 and 4 µg. per ml. When 750 mg. was given 4-hourly, or 1 g. every 6 hours, levels of 4 to 8 µg. were frequently observed. Levels in cerebrospinal fluid of 0.06 to 1.25 µg. per ml. were noted in six out of eight tested. [That aureomycin penetrates into the cerebrospinal fluid is of striking interest.] *R. R. Willcox*

Prophylactic Treatment of Contacts with Syphilis. (Zur Frage der prophylaktischen Behandlung Syphilisgefährdeter.) LÖHE, H. (1948). *Derm. Wschr.*, **119**, 707.

The author holds the view that without definite diagnosis prophylactic measures against syphilis should not be undertaken, because in so many cases infection does not occur after contact with a highly infectious individual. This is illustrated by several case-histories.

Exceptions can be made in the case of marital or engaged partners. An even more definite exception must be made after blood transfusion from a syphilitic donor ; here it is essential to treat the recipient without waiting for any clinical manifestations of syphilis. According to the author this emergency occurs about once in every 4,000 transfusions in Germany. *G. W. Csonka*

Congenital Syphilitic Osteopathy ; Penicillin and Combined Therapy. (Osteopatie da lue congenita e loro terapia penicillinica e mista.) BRUSA, P. (1949). *Minerva pediat.*, 1, 213.

The author gives a brief resumé of work, done chiefly by English and American authors, on the use of penicillin in congenital syphilis with special reference to bony lesions. He describes three types of bony lesion which may occur : (1) osteochondritis ; (2) periostitis ; (3) a fibrosing osteitis, which is less common. English and American workers describe good effects of penicillin alone on these bony lesions, but French authors obtained more favourable results when penicillin administration was combined with arsenotherapy.

The author describes six cases of congenital syphilis, with typical signs, such as rhinitis, macular skin lesions, anaemia, hepatomegaly, and splenomegaly. All had, in addition, clinical and radiological evidence of syphilitic osteopathy, and in all the Wassermann reaction was strongly positive. The ages of the children treated varied between 1 and 3½ months. Radiographs are reproduced. Of the series, three cases were treated with penicillin alone, the average dose being 3,000,000 units. Although there was considerable improvement in the general condition with amelioration of the visceral signs and symptoms, there was little if any change in the bony lesions, as demonstrated radiologically. In the other three cases penicillin therapy was followed by a course of arsenic injections and mercurial inunctions, and in two cases clinical and radiological signs definitely regressed, though in the third case the radiological changes persisted.

The author suggests that the partial failure of penicillin is due to the nature of the blood supply to bone, the antibiotic being destroyed before a therapeutic level is reached at the site of the lesion ; mercury and arsenic, being destroyed less rapidly by the body, have a more efficient action in this respect. *Barbara J. Nathan*

Neurosyphilis : Comparative Treatment with Penicillin Alone and Penicillin Plus Malaria. SPILLER, W. F., and STEWART, J. (1950). *J. invest. Derm.*, 14, 121.

A series of 170 patients with various types of neurosyphilis was treated with penicillin alone or with penicillin plus malaria. Observation extended over periods ranging from 6 months to 4 years or more. In all types the cerebrospinal-fluid response and the symptomatic response were broadly the same with both forms of treatment. *James Marshall*

Tertiary Syphilis : "Acute Swelling of the Testicle" of Ricord. Penicillin ineffective. (Sifilis terciaria ; "fluxion aguda del testículo" de Ricord. Accion nula de la penicilina.) LEDO-DUNIBE, E. (1949). *Actas dermo-sif.*, 41, 221.

Observations on the Treatment and Cure of Reinfections with Syphilis. (Observaciones sobre el tratamiento y curacion de las reinfecciones sifiliticas.) LAZO GARCIA, S. (1949). *Actas dermosif.*, 41, 117.

Tryparsamide and Bismuth Subsalicylate in the Treatment of Experimental Syphilis of Rabbits. Synergistic or Additive Activity. KOLMER, J. A. (1950). *Arch. Derm. Syph.*, Chicago, 61, 271.

Appearance of Generalized Mucocutaneous Secondary Lesions in the Course of Treatment of a Case of Serum-negative Primary Syphilis. Disappearance of Lesions with Arsenoxides Followed by Recurrence. Clinical Cure and Serological Reversal After Penicillin Treatment. Commentary. (Aparicion de un secundarismo cutaneo-mucoso generalizado en pleno tratamiento de una sifilis primaria seronegativa. Blanqueamiento lesional con arsenoxidos y arsenoxidorecidiva posterior. Curacion clinica y negativizacion serologica mediante penicilino-terapia retardada. Comentarios que el caso sugiere.) GONZALEZ CALVO, S. (1949). *Actas dermosif.*, 41, 133.

Arsenoxide in the Treatment of Syphilis. (L'arsenossido nella terapia della sifilide.) SEMMOLA, L., GARDENGHI, G., and RAPACCINI, G. (1948). *G. ital. Derm. Sif.*, 89, 286.

Immediate Results of Treatment of Primary and Secondary Syphilis. (In Russian.) DMITRIEVA, I. N. (1948). *Vestn. Vener. Derm.*, 5, 12.

Capillary Permeability in Patients with Early Syphilis and Influence of Antisyphilitic Therapy Upon it. (In Russian.) TERESHKOVICH, V. I. (1948). *Vestn. Vener. Derm.*, 5, 15.

An Intensive Method of Treatment of Syphilis. (In Russian.) GUREV, A. N., and VALKOV, M. I. (1948). *Vestn. Vener. Derm.*, 5, 8.

Prenatal Prophylaxis against Congenital Syphilis. (Über die prænatale Prophylaxe der Lues congenita.) MAYER-AULL, C. (1948). *Med. Klinik*, 43, 386.

Results of Therapy by Race, Sex, and Stage of Syphilis. BAUER, T. J., and PRICE, E. V. (1949). *J. vener. Dis. Inform.*, 30, 1.

Herxheimer Reactions in Penicillin Treatment of Syphilis in Pregnancy. BOWEN, J. H., COLE, H. N., DRIVER, J. R., LIGHT, R. C., and RAUSCHKOLB, J. E. (1948). *Arch. Derm. Syph.*, Chicago, 58, 735.

SYPHILIS (Pathology)

Studies on Treponemal Immobilizing Antibodies in Syphilis. II. Incidence in Serum and Cerebrospinal Fluid in Human Beings and Absence in "Biologic False Positive" Reactors. NELSON, R. A., ZHEUTLIN, H. E. C., DIESENDRUCK, J. A., and AUSTIN, P. G. M. (1950). *Amer. J. Syph.*, 34, 101.

Examinations for the presence of treponemal immobilizing activity were made on the sera of 81 normal

persons, of 87 patients with diseases other than syphilis, and of 196 patients in various stages of syphilis.

No activity was detected in the serum of normal persons or in cases of non-syphilitic diseases, with the exception of yaws. Of the sera of cases of primary syphilis 23 showed activity, four doubtful activity, and three no activity. In cases of secondary syphilis and in representative groups of cases in the later stages some degree, usually well-marked, of activity was invariably found. The groups comprised 31 cases of secondary syphilis, fifty of latent syphilis, eighteen of asymptomatic neurosyphilis, and 51 of symptomatic syphilis (tabes, paresis, aortitis, aneurysm, and skin lesions).

Strong immobilizing activity was shown by the spinal fluid in all 33 cases of neurosyphilis, but no activity was found in the spinal fluid of any of 25 cases of non-syphilitic diseases.

The immobilizing activity of the serum in cases of late syphilis giving negative serological reactions is of much interest, and seven such cases were investigated. All gave a strong immobilizing reaction.

After adequate study [case histories are given in detail] twelve patients were selected as giving biological false-positive serum reactions, but in no case could any immobilizing activity be detected in the serum.

The authors state that preliminary data on the effect of treatment on the serum of individual patients indicates that in early syphilis there is a decline of immobilizing activity within 6 to 12 months after penicillin therapy, but in cases of late syphilis, within the same period, no decrease was detected.

V. E. Lloyd

Revaluation of Weltmann Serum Coagulation Reaction in Syphilis and Various Dermatoses. GOLDSTEIN, L. (1950). *Arch. Derm. Syph., Chicago*, **61**, 285.

The Weltmann serum coagulation reaction is non-specific; heat coagulation is observed in a certain number of tubes containing mixtures of blood serum and varying concentrations of calcium chloride. The test is of value in differentiating exudative from fibrotic processes and forecasting the course and evolution in many diseases.

Weltmann noted that while normal serum was coagulated by boiling no such reaction occurred when the serum was diluted with 50 parts of distilled water unless an electrolyte was added before boiling. Different dilutions of calcium chloride, varying in each tube by 0.01 per cent. from 0.1 to 0.01 per cent., are mixed in ten tubes with one-fiftieth the volume of serum and the mixtures are boiled. Normally coagulation will constantly take place in a certain number of tubes but in exudative processes, such as pulmonary tuberculosis, there is a shift towards the higher calcium chloride dilutions (shift to the left) while in fibrotic processes, such as cirrhosis of the liver, the shift is towards the lower dilutions (shift to the right).

A shift to the right was noted in six out of ten cases of primary syphilis, in eleven out of fourteen of secondary syphilis, in 25 out of thirty of latent syphilis, in all of five cases of asymptomatic neurosyphilis, and in all of three cases of cardiovascular syphilis. Spinal fluid did not coagulate in any dilution.

Of 42 sera from 130 patients with 38 types of dermatosis, 27.5 per cent. showed a shift towards the higher dilutions, 27.5 per cent. were normal, and a shift to the lower dilutions was noted in 45 per cent. A shift towards the higher dilutions was noted in three cases of chancroid, three out of four of erythema multiforme, two out of four of pemphigus, and one case of lymphatic sarcoma. A shift towards the lower dilutions was observed in all of ten cases of psoriasis, six out of ten of eczematoid dermatitis, all of four of ichthyosis, four out of five of lichen planus, and five out of eight of urticaria.

R. R. Willcox

Multiple Primary Carcinomata of the Skin with Co-existing Tertiary Syphilis. (Über primär multiple Hautcarcinome bei gleichzeitiger tertiärer Lues.) HASSELMANN, C. M., and JOHNE, H. O. (1950). *Arch. Derm. Syph., Wien*, **188**, 693.

A 74-year-old woman suffering from multiple primary carcinomata of the face is described. The co-existing tertiary syphilis and senile keratoses appeared to be aetiological factors. Previous inadequate treatment for the syphilis is regarded as possibly contributing to this outcome, and penicillin is considered to be the drug of choice in all cases of syphilis.

G. W. Csonka

Antagonism Between the Lymphogranuloma Venereum Virus and *Treponema pallidum*. (Antagonisme entre le virus lymphogranulomateux et le *Treponema pallidum*.) LEVADITI, C., and VAISMAN, A. (1950). *Ann. Inst. Pasteur.*, **78**, 404.

Mice were inoculated intracerebrally with the virus of lymphogranuloma venereum and 5 days later when the mice appeared ill they were inoculated intracerebrally with a suspension of *Treponema pallidum*. Mice died in from 2 hours to 9 days after infection or were killed between 26 and 127 days after inoculation. Although the lesions of lymphogranuloma venereum were present it was impossible to determine the presence of *T. pallidum* in either the brain or in other tissues of the body. The reticulo-endothelial lesions in the brain are considered to have inhibited the dissemination and proliferation of the spirochaetes. There is no interference between *T. pallidum* and *Spirochaeta duttoni* in the mouse.

G. M. Findlay

Filter Paper Microscopic Test for Syphilis, or the FPM Test. A Preliminary Report. HOGAN, R. B., and BUSCH, S. (1950). *J. vener. Dis. Inform.*, **31**, 37.

A Comparison of the Wassermann and Kahn Reactions. OSMOND, T. E. (1950). *Brit. med. J.*, **1**, 524.

GONORRHOEA (Therapy)

Treatment of Gonorrhoea with Oral Penicillin. JACOBY, A., and OLLSWANG, A. H. (1950). *Amer. J. Syph.*, **34**, 60.

A study is briefly reported of the treatment of gonorrhoea with penicillin by mouth in a New York Clinic. There were 284 males and 25 females; infection was diagnosed by smear and culture, being acute in th

majority of cases. Tablets of crystalline penicillin G buffered with glycerides and sodium salts of fatty acids or with aluminium hydroxide were used, the dosage ranging from 100,000 to 600,000 units. In many cases treatment was given as a single dose before the patient left the clinic. The disappearance of symptoms and the finding of three successive negative smears and cultures at weekly intervals were considered to represent a cure. When less than 400,000 units were given no cures resulted. When the dose ranged from 400,000 to 600,000 units, 82 to 84 per cent. of males and 72 to 100 per cent. of females were cured. Studies of penicillin level in the blood in these cases are recorded and it is believed that oral penicillin will prove "a practical, painless, and satisfactory therapeutic procedure."

S. M. Laird

The Use of Dihydrostreptomycin in the Treatment of Gonorrhea. TAGGART, S. R., PUTNAM, D. E., GREAVES, A. B., and WATSON, J. A. (1950). *Amer. J. Syph.*, 34, 62.

Streptomycin in doses of 0.3 to 0.6 g. has cured gonorrhoea in some 90 per cent. of cases. Dihydrostreptomycin is here reported to have cured 95 out of 104 cases of gonorrhoea in the male when given as a single injection of 0.2 to 0.4 g. Smaller dosage was unsuccessful. Some transitory pain at the site of injection was the only reaction noted.

S. M. Laird

Aureomycin in the Treatment of Gonorrhea in the Male.

ROBINSON, R. C. V. (1950). *Amer. J. Syph.*, 34, 64.

Aureomycin promises to prove useful in all the venereal diseases. Earliest American reports indicated that it was effective in gonorrhoea, although to a lesser degree than penicillin; the present report confirms this view. Gonorrhoea in 77 males was treated with a single dose of aureomycin taken by mouth under supervision. The first seven patients received 0.5 g. only and in three the treatment failed. The remaining seventy patients were each given 1 g. (four 250 mg. capsules) and 56 (80 per cent.) were considered cured. The urethral discharge abated within 10 to 24 hours. The author believes that re-infection and alcohol consumption may have been responsible for some failures, but that aureomycin given as described is less effective than 75,000 units of procaine penicillin in oil.

S. M. Laird

Treatment of Gonorrhoea in Women by the Local Submucous Injection of Penicillin; Control of Results by Gonococcal Culture. (Traitement de la blennorragie féminine par les injections pénicillinées locales sous-muqueuses. Contrôle des résultats par la culture du gonocoque.) DEBRAY, J. R. (1949). *Pr. méd.*, 57, 1134.

This technique was developed as a result of the observation that the standard treatment of gonorrhoea by penicillin was much less effective in women than in men. With a fine dental needle, six to eight submucous injections of 1.5 ml. penicillin solution (500,000 units in 20 ml. saline) are made within the cervical canal. Four injections are given around the urethra, a surface analgesic being previously used. If there is evidence of

infection of the glands of Skene or Bartholin, local injections are given. In the first instance treatment is given every other day for 8 days, but it may be continued if the results are not then satisfactory. Penicillin in aqueous solution (400,000 units in two doses, morning and evening) is also injected intramuscularly on the first and last days of treatment, and 3 g. sulphathiazole is given daily for the first 3 days. Results are controlled by cultures and have been markedly better than with standard treatment alone.

James Marshall

Gonococcal Arthritis: A Study of 202 Patients Treated with Penicillin, Sulfonamides or Fever Therapy.

ROBINSON, J. A., HIRSH, H. L., ZELLER, W. W., and DOWLING, H. F. (1949). *Ann. intern. Med.*, 30, 1212.

The results of treatment in 202 cases of proved gonococcal arthritis at the Gallinger Municipal Hospital, Washington, over the past twelve years are reviewed. In this series, 109 patients (53.9 per cent.) were males, and 93 (46.1 per cent.) females. The condition was poly-articular in 163 cases.

Fever therapy was employed in 55 cases. After use of the Kettering hypertherm, 21 out of 33 patients (63.6 per cent.) were cured, whereas intravenous typhoid vaccine was found to be much less satisfactory. Various types of sulphonamides were used in 140 cases, with cure in 69.3 per cent.). The type of sulphonamide used appeared to have little effect on the results of treatment, but the larger doses over a longer period used in later years seemed more effective. Penicillin therapy was used in 32 patients, of whom 71.8 per cent. were cured, but in some of the early cases of failure the dosage was probably inadequate.

In all forms of treatment used, the "acute" cases, with symptoms for less than 30 days, responded more favourably than the "chronic" ones. The authors conclude that penicillin is the drug of choice in the treatment of gonococcal arthritis, and recommend a total of 2 to 5 million units over a period of five to ten days. In the more chronic type of case, where no response is obtained to penicillin, fever therapy is sometimes more effective.

Kathleen M. Lawther

Ophthalmia Neonatorum and Gonococcal Conjunctivitis.

McEvoy, J. P. (1950) *Eye, Ear, Nose, Thr. Mou.*, 28, 25.

GONORRHOEA (Pathology)

Gonorrhea Complicating Pregnancy and its Relation to Ophthalmia Neonatorum. BERNSTEIN, J. B., and BLAND, G. W. (1948). *Urol. cutan. Rev.*, 52, 464.

OTHER VENEREAL DISEASE CONDITIONS

The Laboratory Diagnosis of Lymphogranuloma Venereum.

BEDSON, S. P., BARWELL, C. F., KING, E. J., and BISHOP, L. W. J. (1949). *J. Clin. Path.*, 2, 241.

Lymphogranuloma venereum is diagnosed by the finding of the specific virus, but, as this is a time-consuming procedure, the authors have re-investigated

the value of the Frei test and the complement-fixation reaction.

The antigen for the complement-fixation test was prepared from yolk-sac cultures, and was subjected to steaming, which destroyed the heat-labile antigenic components. With such an antigen a positive complement-fixation test at 1 in 32 was obtained in 87.5 per cent. of 32 cases in which a "confident" clinical diagnosis had been made, in 22.6 per cent. of 31 cases in which the diagnosis was "possible", and in 1.5 per cent. of cases in which the clinical diagnosis was "doubtful". Thus the serological findings showed quite a close correlation with the clinical diagnosis.

The effective antigen in this complement-fixation test is the heat-stable one also found in psittacosis, so that the test is positive also in cases of the latter disease.

Psittacosis virus contains a heat-labile antigen in addition to the stable group-specific component, and there is evidence that the viruses of psittacosis and lymphogranuloma venereum each possess a specific antigen detectable by neutralization tests made with antisera produced in the domestic fowl. Neutralization tests made with human and mammalian sera give no such clear-cut specificity, however. But there is some evidence that mammalian anti-psittacosis sera do contain antibody to the labile antigen, so an attempt was made, on analogy, to demonstrate complement fixation with fresh, unheated lymphogranuloma venereum virus. No success was obtained.

It has been shown that if a psittacosis antiserum made in the guinea-pig be absorbed with steamed psittacosis antigen the corresponding antibody is removed, leaving only the antibody to the heat-labile antigen, whereas absorption with the untreated virus removes both. Thus in the same way treatment of serum from a patient with lymphogranuloma venereum with steamed virus should remove its ability to react not only with the steamed homologous virus but also with both forms of heterologous virus. This the authors found to be the case.

The Frei test was also carried out in the great majority of the cases examined serologically, the effective antigen again being a heat-stable one. There was a close parallelism between the Frei reaction and the complement-fixation reaction in the clinically positive group; in a considerable number of doubtful cases of lymphogranuloma venereum there was a strongly positive Frei reaction but there was little or no antibody in the serum. These were thought to be old cases in which the disease was now quiescent.

As was anticipated, intracutaneous tests made with steamed psittacosis virus on 39 patients gave similar results to that of the Frei test. An attempt was made to elaborate a specific skin reaction by treating suspensions of psittacosis virus and lymphogranuloma venereum virus with acid, in order to inactivate the heat-stable components. Parallel tests were then carried out in a small number of cases. While the acid-soluble antigen of psittacosis virus failed to produce a reaction in these cases of lymphogranuloma venereum, the homologous extract elicited a definite response. In one case of psittacosis the results of using these preparations were equally specific.

R. B. Lucas

The Treatment of Bacillary Urinary Infections with Chloromycetin. CHITTENDEN, G. E., SHARP, E. A., VONDER HEIDE, E. C., BRATTON, A. C., GLAZKO, A. J., and STIMPERT, F. D. (1949). *J. Urol.*, 62, 771.

The results of treatment with "chloromycetin" (chloramphenicol) in fifty patients with urinary infection are described. In the majority of cases mixed infection was present in association with a variety of obstructive and other pathological lesions. In consequence, the need for "adjunct treatment" with penicillin and sulphonamides or for surgical intervention was frequently recognized and the therapeutic response became correspondingly difficult to assess. In a high proportion of high Gram-negative infections, however, sustained improvement followed the use of chloromycetin. Oral doses of 0.25 to 0.5 g. at 6- to 8-hourly intervals were found most effective and were unaccompanied by gastrointestinal, neurotoxic, cutaneous, or allergic reactions. Chemical and biochemical assays of the antibiotic in the serum usually showed satisfactory concentration soon after administration, though in a few cases absorption was slow. Similar assays on the urine indicated the presence of a high proportion of inactive metabolic products of chloromycetin, with only about 15 per cent. of the antibiotic remaining active on excretion.

J. D. Fergusson

Streptomycin in Soft Sore. Observations on Clinical and Experimental Infections. WILLCOX, R. R. (1950). *Lancet*, 1, 396

It has been known for several years that *Haemophilus ducreyi* is sensitive to streptomycin. The author records the satisfactory therapeutic effect of the antibiotic on seven male African negroes who were suffering from chancroid. A total dose of 2 to 4.5 g. (0.5 or 1 g. daily for 4 to 9 days) was sufficient to heal the lesions within 3 to 12 days. Relapse occurred in one patient, whose chancroid had healed after three daily injections of 0.5 g. of streptomycin. He returned 17 days later and the sores healed after a further course of 0.5 g. daily for 4 days. Injection into volunteers of bubo fluid from persons treated with streptomycin provoked no reaction, nor did the injection of fluid from untreated donors into volunteers given 1.5 to 6 g. of streptomycin over 2 to 5 days. This suggests that the drug is also prophylactic. Nevertheless, the author considers that the sulphonamides are to be preferred in the treatment of chancroid as they are just as effective as streptomycin and do not mask a possible co-existing syphilitic infection.

T. Anwyl-Davies

Treatment of Lymphogranuloma Venereum with Aureomycin. ROBINSON, R. C. V., ZHEUTLIN, H. E. C., and TRICE, E. R. (1950). *Amer. J. Syph.*, 34, 67.

The isolation of the causative virus in lymphogranuloma venereum is difficult, and the diagnostic criteria adopted in the series of nine cases reported herewith comprised a positive intradermal reaction with "lygranum" antigen and a positive lymphogranuloma complement-fixation reaction. Eight patients were Negroes and all nine had clinical signs including buboes or proctitis.

Four patients received aureomycin intramuscularly (0.56 to 3.6 g. in 4 to 15 days) but pain at the site of injection was so great that the oral route (3.6 to 38.0 g. in 5 to 15 days) was used in subsequent patients. Measured by healing of genital lesions, reduction in size or complete resolution of buboes, or improvement of proctitis judged by proctoscopic examination, results were not impressive. Only three patients showed any definite improvement.

S. M. Laird

A Five Day Peroral Treatment of Yaws with STB, a New Trivalent Arsenical. FRIEDHEIM, E. A. H. (1949). *Amer. J. trop. Med.*, **29**, 185.

A drug for the mass treatment of yaws in the less developed parts of the tropics should be cheap, chemically stable, safe, easily administered, and effective in a short course of treatment; for these reasons the author commends the 3-weeks' course of injections of acetarsol and bismuth salicylate of the Sierra Leone Health Service, although effective oral treatment would be preferable. He has prepared a relatively non-toxic and stable tervalent derivative of acetarsol, named "STB", which is 4-oxy-3-acetylaminophenylarsenoxide. It was tested in 88 cases of yaws in the district of Gueckedou, French Guinea, 73 of these being of the infectious type and fifteen non-infectious (crab yaws); each patient was given by mouth a daily dose of 0.01 to 0.02 g. per kg. body weight for 5 days. Exudative lesions were epithelized by the fifth day, crevasses and fissures had healed, and the soles of the feet had become painless and non-sensitive in many cases; 3 months after treatment 87 patients out of 88 were cured. Similar results were obtained in 75 cases of yaws in the Belgian Congo; all the patients except one were clinically cured one month after treatment, and after 5 months 69 were still clinically cured while five had relapsed. The drug caused no untoward effects.

J. F. Corson

Recent Observations on Granuloma Inguinale, with Report on Streptomycin Therapy. CHEN, C. H., GREENBLATT, R. B., and DIENST, R. B. (1948). *Arch. Derm. Syph., Chicago*, **58**, 703.

Reiter's Disease as a Venereal Disease. (Morbus Reiter—eine Geschlechtskrankheit?) LÖVGREN, O., and MASRELIEZ, N. (1949). *Z. Rheumaforsch*, **8**, 234.

The Newer Antibiotics in the Therapy of the Venereal Diseases Other than Syphilis. GREENBLATT, R. B., WAMMOCK, V. S., CHEN, C. H., DIENST, R. B., and WEST, R. M. (1950). *J. vener. Dis. Inform.*, **31**, 45.

MISCELLANEOUS

The Use of Bismuth Salts in the Treatment of Sporadic Goiters. VILLAYERDE, M. (1949). *J. clin. Endocrinol.*, **9**, 462.

During the treatment of syphilitic patients with bismuth salts it was observed that certain of them had goitres and that these decreased in size. A series of patients with goitre were therefore given routine anti-

syphilitic treatment. They received from one to three courses of twenty injections, at weekly or twice-weekly intervals, of either bismuth subsalicylate 0.13 g. or bismuth heptadiencarbonate 0.045 g. Of diffuse goitres in ten patients, five were greatly improved, two slightly improved, and three showed no change. Of nodular goitres in six patients, three were much improved and one only slightly, and two showed no change. In general the best results were obtained with patients who had had the longest treatment. Bismuth salts had no effect on thyrotoxicosis.

A. C. Crooke

Arsenical Encephalopathy Treated with BAL. (Encefalopatía arsenical tratada con BAL.) GOMEZ ORBANEJA, J., and RISCO, A. (1949). *Actas dermo-sif.*, **40**, 783.

The patient, a man of 22, had serum-negative primary syphilis and had received a total of 5.70 g. neoarsphenamine and 1.27 g. bismuth metal over a period of about 6 weeks when he developed symptoms and signs typical of severe arsenical encephalopathy. The cerebrospinal fluid gave a positive reaction for globulin and contained 50 cells per c.mm. He was treated with 4 ml. (200 mg.) BAL, every 4 hours for eight doses, and then at longer intervals to a total dose of 2.8 g. He was also given aneurin and magnesium sulphate intravenously on two occasions. Improvement began after the second BAL injection, and complete recovery ensued. *James Marshall*

Reevaluation of Penicillin Dosage Schedules. ALTEMEIER, W. A. (1948). *Arch. Surg., Chicago*, **57**, 396.

A study of the effectiveness of penicillin injected in doses of either 100,000 units 8-hourly or 150,000 units 12-hourly in 87 selected cases is discussed in this paper. Alternative methods of avoiding frequent injection are considered, namely, by delaying absorption by giving the penicillin in oil or beeswax, by delaying excretion by the administration of caronamide, and oral administration. It is pointed out that whatever method is used the maintenance of an adequate level in the blood will ensure efficient therapy. However, evidence is accumulating that maintenance of this therapeutic level may not be essential and that the bacteriostatic effect of penicillin persists after its disappearance from the blood.

From the evidence of this small series it appears that the maintenance of a constant level in the blood is unnecessary for the treatment of moderately severe infections, as in cases in which penicillin was not detectable in the blood for 5 hours out of every 8 during treatment the results obtained were indistinguishable from those obtained where a higher blood penicillin level was maintained throughout. The author stresses that 8-hourly doses should only be used in cases of moderate infection until further experimental information is gathered.

A. J. Drew

CORRECTION

Vol. XXVI, No. 2, p. 105.

The article, "Urethritis, Gonococcal and Non-Specific, Treated by Aureomycin" (1949), *Brit. med. J.*, **2**, 257, was written by R. R. Willcox and G. M. Findlay, and not by R. R. Willcox as stated.